PART I: AN ABNORMAL REACTION IN THE SOMMELET ALDEHYDE SYNTHESIS

PART II: THE COUPLING ACTION OF THE GRIGNARD REAGENT AND THE ORTHO EFFECT

BY

JACK JOE DENTON

B.S., Oklahoma A. and M. College, 1937

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
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PART I
AN ABNORMAL REACTION IN THE SOMMELET ALDEHYDE SYNTHESIS

INTRODUCTION

The publication of the original work on the Sommelet aldehyde synthesis was followed immediately by a paper in which mention was made of the preparation of mesitaldehyde by this method.[1] Other authors have indicated more recently that the decomposition of hexamethylenetetrammonium salts in a manner similar to that outlined by Sommelet gave nitrogen-containing compounds. The apparent contradiction of these two results and the desire for a new synthesis of mesitaldehyde have led to the study of the decomposition of α^2-isodurylhexamethylenetetrammonium chloride.

EXPERIMENTAL AND DISCUSSION OF RESULTS

The α^2-chloroisodurene(I) was obtained by the chloromethylation of mesitylene according to the directions of Nauta and Dienske.[2] The chloro compound(1) was condensed with hexamethylenetetramine, and the resulting α^2-isodurylhexamethylenetetrammonium chloride was decomposed in aqueous solution according to the procedure of Sommelet.[1] Instead of the expected mesitaldehyde there was formed a white solid base, m.p. 151.5-152°, which proved to have the formula $C_{21}H_{30}N_2$. A Zerewitinoff determination showed the presence of two active hydrogen atoms. The most probable structure appeared to be that given in formula II.

$C_9H_{11}CH_2Cl$ — I

$C_9H_{11}CH_2NHCH_2NHCH_2C_9H_{11}$ — II

Evidence has been accumulated which establishes the correctness of this formula. Acetylation and benzoylation of N,N′-di-α^2-isodurylmethanediamine(II) yielded N-α^2-isodurylacetamide ($CH_3CONHCH_2C_9H_{11}$) and N-α^2-isodurylbenzamide ($C_6H_5CONHCH_2C_9H_{11}$), respectively. The structures of these two amides were confirmed by synthesis from the parent amino compound, α^2-isodurylamine ($C_9H_{11}CH_2NH_2$).

This amine (isolated as its hydrohalide) was prepared in three different ways. Mesitonitrile, made from bromomesitylene by the Rosenmund-von Braun method,[3] gave a high yield of the amine when hydrogenated at high pressure in the presence of Raney

nickel. This synthesis is remarkable in that it involves hydrogenation of a highly hindered nitrile. A second method was that of Delépine [4] which consisted in decomposing α^2-isodurylhexamethylenetetrammonium chloride by means of alcoholic hydrogen chloride. Finally, α^2-chloroisodurene was transformed into the amine by the Gabriel phthalimide method. The N-α^2-isodurylphthalimide was hydrolyzed by heating with a mixture of hydrobromic acid, glacial acetic acid, and acetic anhydride.

That the product obtained by the Sommelet procedure was in fact N,N′-di-α^2-isodurylmethanediamine(II) was proved by the discovery that it could be made readily by allowing either formaldehyde or hexamethylenetetramine to act upon the hydrochloride of α^2-isodurylamine. Moreover, hydrolysis of the diamine(II) with dilute hydrochloric acid gave formaldehyde (identified as its methone derivative) and the hydrochloride of α^2-isodurylamine.

SUMMARY

An attempt to prepare mesitaldehyde from α^2-chloroisodurene and hexamethylenetetramine by the method of Sommelet led to anomalous results. The product has been shown to be N,N′-di-α^2-isodurylmethanediamine.

Formaldehyde was identified as a degradation product of the diamine on acid hydrolysis. N-α^2-Isoduryl-acetamide and -benzamide, respectively, were obtained by acetylation and benzoylation of the diamine. The structure of these amides was proved by synthesis.

The diamine was synthesized by reaction of either formaldehyde or hexamethylenetetramine with α^2-isodurylamine hydrohalide. The latter was prepared in three different ways: the hydrogenation of mesitonitrile, the Gabriel method, and the Delépine method. The Rosenmund-von Braun method has been applied to the synthesis of mesitonitrile.

While no satisfactory mechanism has been developed for the normal course of the Sommelet synthesis of aldehydes from the corresponding alkyl halides, it appears that it involves at least one step which is inhibited by the mesityl radical.

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PART II

THE COUPLING ACTION OF THE GRIGNARD REAGENT AND THE ORTHO EFFECT

INTRODUCTION

The Grignard reagent causes certain alkyl and aralkyl halides to undergo a coupling reaction in the manner of the Wurtz synthesis, with the Grignard reagent playing the role of the metal. This coupling reaction occurs simultaneously with alkylation of the halogen compound either as a major or side reaction. The effect of the added factor of steric hindrance on the course of this reaction has, however, never been studied. Since the arylmethyl halides appear to be most suitable for this coupling reaction, and since the course of the reaction for the simple members of this class has been reported, di-ortho-substituted arylmethyl halides were considered ideal for observing the effect of possible steric hindrance in this coupling reaction.

EXPERIMENTAL AND DISCUSSION OF RESULTS

Three arylmethyl halides were submitted to the coupling action of the Grignard reagent: α^2-chloroisodurene, 2,6-dimethyl-4-*t*-butylbenzyl chloride, and mesital chloride. Methylmagnesium iodide was selected as probably the most effective Grignard reagent for the coupling reaction.

The methyl groups in the ring of α^2-chloroisodurene enhance the activity of the halogen atom, measured by the equivalent conductance in liquid sulfur dioxide as observed by Nauta and Dienske,[1] to ten times that of benzyl chloride itself. Besides the enhanced activity of the halogen comes also the added factor of the possible steric hindrance of the two ortho methyl groups. With these two factors opposing one another the yield of coupled product from α^2-chloroisodurene as compared with that from benzyl chloride should indicate the extent of the steric hindrance in such a coupling reaction. When α^2-chloroisodurene was added to a solution of methylmagnesium iodide, *s*-dimesitylethane [2] was obtained in a yield of 86 per cent. The only other product of the reaction was ethylmesitylene. This result showed that the ortho methyl groups offered no appreciable opposition to the coupling since benzyl chloride,[3] itself, yielded only 75 per cent of coupled product. Tetrabromo-*s*-dimesitylethane [2] and dinitroethylmesitylene [4] were made.

Likewise, 2,6-dimethyl-4-*t*-butylbenzyl chloride was found to give a yield of 85 per cent of the coupled product, 1,2-di-(2,6-dimethyl-4-*t*-butylphenyl)ethane and a small amount of 1,3-dimethyl-2-ethyl-5-*t*-butylbenzene, the alkylation product. The ethane, a new compound, was identified as its dibromo and tetranitro derivatives.

Mesital chloride was prepared according to the directions of Asinger and Lock [5] from mesitaldehyde and phosphorus pentachloride. When subjected to a coupling reaction with methylmagnesium iodide, mesital chloride gave *s*-dimesitylethylene as the only identified product in a yield of about 30 per cent. It was assumed to be the *trans* form since it corresponded closely in physical properties with *trans*-stilbene. It was synthesized by two other independent methods.

A magnesium-magnesium iodide mixture coupled mesital chloride to *s*-dimesitylethylene which was identical with that from the coupling action of the Grignard reagent.

Desoxymesitoin [6] was hydrogenated quantitatively in a pressure bomb in the presence of copper chromite to 1,2-dimesitylethanol. This ethanol could be smoothly dehydrated either by acetic anhydride or by phosphorus pentoxide, suspended in benzene, to give *s*-dimesitylethylene.

SUMMARY

α^2-Chloroisodurene has been found to give a good yield of the coupling product, *s*-dimesitylethane, and a small amount of the alkylation product, ethylmesitylene, when treated with methylmagnesium iodide.

Likewise, 2,6-dimethyl-4-*t*-butylbenzyl chloride has given a good yield of 1,2-di-(2,6-dimethyl-4-*t*-butylphenyl)ethane and a small amount of 1,3-dimethyl-2-ethyl-5-*t*-butylbenzene.

Mesital chloride, when treated with the same Grignard reagent, has yielded *s*-dimesitylethylene as the only identified product.

From these studies it has been concluded that the ortho methyl groups not only offer little hindrance to the coupling action of the Grignard reagent but actually seem to favor it.

s-Dimesitylethylene has been synthesized by two other independent methods: first, the action of a magnesium-magnesium iodide mixture on mesital chloride; second, the dehydration of 1,2-dimesitylethanol. The ethanol has in turn been prepared by the hydrogenation of desoxymesitoin.

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VITA

The author was born November 24, 1915, in Newkirk, Oklahoma. He attended the public schools of that town, graduating from Newkirk High School in 1933. Oklahoma Agricultural and Mechanical College at Stillwater, Oklahoma, was the school in which he enrolled in 1933; he received the degree of Bachelor of Science from this college in 1937. He entered the University of Illinois in September, 1937. During the school years of 1937-1940 he held a teaching assistantship at this university, and for the year 1940-1941, a special research assistantship.